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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/605,577	06/28/2000	Wei Wang	MSB-7267	5817

7590 01/14/2003
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EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	PAPER NUMBER

1647
DATE MAILED: 01/14/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

PLUGBY

Office Action Summary	Application No.	Applicant(s)	
	09/605,577	WANG ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 September 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This office action is in response to the amendment and response filed on 9/27/02 in Paper No: 16. Pending claims 1-6 and 9-19 have been cancelled and replaced with new claims 11-17.
2. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.
3. The declaration provided by Dr, Wei Wang is acknowledged.

Claim Objections

4. Claims 12-17 are objected to because they depend on rejected claim 1.

Claim Rejections - 35 USC § 102, withdrawn

5. The rejection of claim 1 under 35 USC 102(b) as being anticipated by Patel et al is withdrawn because claim 1 has been cancelled. In addition, the claims are directed to IL-2 and the reference teaches the stabilization of IL-4. Although, there exists difference between aqueous protein stabilization and lyophilized protein stabilization one of skilled in the art would recognize the differences between the methods and it would be obvious for example to lyophilize aqueous compositions (see Andya et al. U. S. Patent No: 6,267,958 column 1, lines 41-50 and Pikal (1990)). However, Applicants arguments with respect to "teaching away" of Patel et al. with respect to stabilization using histidine is persuasive. Therefore, the 35 USC 102(b) rejection is withdrawn.

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Claim Rejections - 35 USC § 103, withdrawn

6. Rejection of claims 1-3, 5 and 9 under 35 U.S.C. 103(a) as being unpatentable over Patel et al. (U.S. Patent No: 5,358, 708) in view of Hora et al. (U.S. Patent No. 5,078,997) is withdrawn because Applicant has elected to cancel claims 1-3, 5, 9 and for reasons stated above in paragraph 4. Furthermore, the newly added claims 11-17 are directed to lyophilized pharmaceutical compositions comprising histidine, glycine and sucrose that were not present in the original set of claims. Therefore, the 35 USC 103 rejection is withdrawn.

Claim Rejections - 35 USC § 103, withdrawn

7. Claims 1-6 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patel et al. (U.S. Patent No: 5,358, 708) and Hora et al. (U.S. Patent No. 5,078,997) in view of Yasushi et al. (U.S. Patent No: 4,645,830) is withdrawn because Applicant has elected to cancel claims 1-6 and 9 and for reasons stated above in paragraphs 4 and 5.

Claim Rejections - 35 USC § 103, withdrawn

8. Claims 1-6, 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patel et al. (U.S. Patent No: 5,358, 708) and Hora et al. (U.S. Patent No. 5,078,997) in view of Yasushi et al. (U.S. Patent No: 4,645,830) and further in view of Shanafelt et al. (WO 996018A1) is withdrawn because Applicant has elected to cancel claims 1-6, 9 and 10 and for reasons stated above in paragraphs 4 and 5.

9. The following are new grounds of rejection necessitated by Applicant's submission new claims.

Claim Rejections - 35 USC § 112

10. Claims 11-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10a. Claim 11-17 are rejected as vague and indefinite for reciting the term "mutein", because the specification does not clearly define the term "mutein". The muteins described could be deletion, substitution, addition of a single amino acid or more than one amino acid.

10b. Claims 12 and 17 are rejected as vague and indefinite for reciting the term "N88R" because the full meaning of an acronym should be spelled out at its first use in any claim.

Claim Rejections - 35 USC § 103

11. Claims 11-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andya et al. (U.S. Patent No: 6,267,958) in view of Shanafelt et al. (WO 996018A1).

The instant invention is directed a pharmaceutical composition comprising human IL-2 or a variant stabilized with amino acids, sucrose and salt.

Andya et al describes a stable lyophilized protein pharmaceutical formulation that can be reconstituted with a suitable diluent to generate a high protein concentration reconstituted formulation. This invention provides a lyophilized protein formulation that

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is stable upon storage and delivery. It also describes a stable reconstituted protein formulation that is suitable for administration (column 1, lines 52-55). It further describes lyophilized formulations that contain protein at concentrations of 2mg/ml to about 50mg/ml (column 14, lines 64-65). The reference further teaches that the protein may be present in a pH buffered solution at a pH about 4-8 meeting the limitation of claim 16 (pH about 5.0 to 6.5). The buffering is typically accomplished by histidine from about 1mM to about 20 mM (column 15, lines 1-10). This is about 0.013% to 0.27 % wt, which is within the limitations of claim 13 (0.06-1.8 % wt). The reference also discloses the use of a bulking agent such as glycine in the concentration of 25mM-266.4mM (column 15, lines 60-65 and Table 2). This represents concentration of about 0.14%-1.5% wt, which is within the limitation of claim 14 (1-3 % wt). The reference uses sucrose in the concentration 10mM-400mM as lyoprotectant (column 15, lines 10-25). This represents concentration of about 0.3%-13.6% wt, which is within the limitation of claim 15 (0.5-3 % wt). Finally with respect to a limitation present in claim 17 that the composition contain 0-0.9 % by wt of NaCl, this limitation is also met by the reference because the composition could contain no NaCl. However, Andya et al. does not explicitly recite a pharmaceutical composition comprising human IL-2 mutein stabilized with amino acids and sucrose.

Shanafelt et al. discloses both the IL-2 and the N88R variant of IL-2 in pharmaceutical compositions for therapeutic uses (page 6, lines 25-30). Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made to stabilize the interleukins disclosed in Shanafelt et al., utilizing amino acids, and

sucrose described in Andya et al. in the concentration ranges as claimed, to produce stabilized interleukins for pharmaceutical formulation, because the reference teaches that the stabilized proteins including interleukins can be lyophilized and then reconstituted with little loss in activity (column 7, lines 1-15). Thus the claimed invention would have been *prima facie* obvious as a whole at the time the invention was made, especially in the absence of evidence to the contrary. Therefore, the instant invention is obvious over Andya et al. (6,267,958) in view of Shanafelt et al. (WO 996018A1). Furthermore, Applicant's arguments against previous art rejections as directed to stabilization of aqueous formulations are moot because Andya et al. reference clearly teaches the stabilization of lyophilized protein formulations.

12. No claims are allowable.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 703-305-1112. The examiner can normally be reached on M-F: 8:30-4:30.

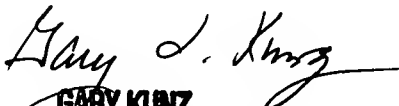
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and 703-308-4227 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

JS

January 10, 2003


GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600